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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,249	11/10/2000	Alan H. Lazarus	701826-050990	3430

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Nixon Peabody LLP
101 Federal Street
Boston, MA 02110

EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	7

DATE MAILED: 05/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/709,249	Lazarus et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 6, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election of the antibody species L368 in Paper No. 6 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-5 are pending and being acted upon.

3. The specification is objected to for the following informalities, β2-microglobulin is misspelled in a number of different ways in the specification. See for example, B-2 microglobulin (page 4), B-2M (page 5), β2M (page 11), $_2$M (page 14), etc.

Appropriate corrections are required.

4. Claims 1-4 are objected to because of the following informalities:

A) in Claims 1, 3, and 4, the phrase "an HLA alloimmune response from said patient," would more properly be written, "an HLA alloimmune response in said patient."

B) in Claim 2, the phrase "wherein said at least one monoclonal antibody is," would more properly be written, "wherein said at least one monoclonal antibody is selected from the group consisting of."

C) in Claim 3, the phrase "transfusing with the presensitizes platelets of step a) to a patient," would more properly be written, "transfusing the presensitizes platelets of step a) into a patient."

D) in Claim 4, the phrase "at least two transfusions from said patient," would more properly be written, "at least two transfusions into said patient."

Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 2, and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a method for inhibiting an HLA autoimmune response to platelet transfusion,
does not reasonably provide enablement for,
a method for preventing an HLA autoimmune response to platelet transfusion or preventing refractoriness to subsequent transfusions.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding "preventing" an alloimmune response or "preventing" refractoriness to subsequent transfusions, "prevent" is defined as an absolute term. To prevent is to keep from happening or to stop (Webster's Ninth New Collegiate Dictionary, 1990). It is disclosed in the specification, however, that the method of the instant claims functions only to inhibit an alloimmune response. See for example, the section at page 7, **Monoclonal HLA-A2 antibody-treated platelets inhibit alloantibody production**, or the section at page 9, **Monoclonal antibodies to HLA Class I, but not to platelet-specific antigens, inhibit the alloimmune response.** Further, the data disclosed in Figure 3 discloses a reduction in the alloimmune response, but not an absolute prevention of said response. Thus, the use of the method of the instant claims for the prevention of an alloimmune response, or the prevention of refractoriness to subsequent transfusions, must be considered highly unpredictable. Given said unpredictability, significant working examples would be required. As the relevant working example (results disclosed in Figure 3) indicates that the claimed method inhibits, but does not prevent an alloimmune response, the claimed method must be considered to require undue experimentation as there would be no particular expectation of success in achieving an absolute prevention of an alloimmune response or prevention of refractoriness to subsequent transfusions.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In view of the quantity of experimentation necessary and the lack

of sufficient working examples, it would take undue trials and errors to practice the claimed invention.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crow et al. (March 1999, IDS) in view of Damjanovich et al. (1995) and Shalit et al. (1985).

Crow et al. teaches a method for inhibiting HLA alloimmune response to platelet transfusion, said method comprising the step of presensitizing platelets with a polyclonal antibody against HLA, a portion thereof, or β2-microglobulin, wherein said platelets if administered to a patient inhibit an HLA alloimmune response in said patient (see particularly page 921, Results, Pretreatment of platelets with an anti-HLA alloantibody reduces their immunogenicity and Figure 1). Further, the reference teaches the inhibition of an alloimmune response after at least two transfusions (see particularly page 923, column 1, 7th paragraph).

The reference differs from the claimed invention in that it does not teach the use of the anti-β2-microglobulin antibody L368 in the claimed method.

Damjanovich et al. teaches that L368 is an anti-β2-microglobulin monoclonal antibody (see particularly page 1122, column 2, **Monoclonal Antibodies**).

Shalit et al. teaches that monoclonal antibodies are more specific, more sensitive, and more accurate than polyclonal antibodies (see particularly Abstract and page 878, column 2, first paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform method for inhibiting HLA alloimmune response to platelet transfusion, said method comprising the step of presensitizing platelets with an antibody against HLA, a portion thereof, or β2-

microglobulin, wherein said platelets if administered to a patient inhibit an HLA alloimmune response in said patient and the inhibition of an alloimmune response after at least two transfusions, as taught by Crow et al., substituting the L368 anti-β2-microglobulin antibody as taught by Damjanovich et al., for the polyclonal antibody taught by Crow et al. One of ordinary skill in the art at the time the invention was made would have been motivated to make said substitution because monoclonal antibodies are more specific, more sensitive, and more accurate than polyclonal antibodies, as taught by Shalit et al.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
May 16, 2002